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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/924,946	08/08/2001	Mark J. Evans	0630/1G703US2	3104

7278 7590 03/08/2006

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EXAMINER	
PAK, YONG D	
ART UNIT	**PAPER NUMBER**
1652	

DATE MAILED: 03/08/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/924,946	EVANS ET AL.	
	Examiner	Art Unit	
	Yong D. Pak	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 December 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *69-95* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *69,72,77 and 81* is/are allowed.

6)☒ Claim(s) *70,71,73-76,78-80 and 82-85, 87-95* is/are rejected.

7)☒ Claim(s) *86* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The amendment filed on December 6, 2005, canceling 8-15, 17-29, 37-41 and 45-68 and adding claims 69-95, has been entered.

Claims 69-95 are pending and are under consideration.

Response to Arguments

Applicant's amendment and arguments filed on December 6, 2005, have been fully considered and are deemed to be persuasive to overcome the rejections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 82-85 and claims 86-89 depending therefrom are rejected under 35 U.S.C. 101 because the claimed invention is directed to a non-statutory subject matter.

Claims 82-85, as written, is directed to non-statutory subject matter. Claims 82-85 could read on a host cell still attached to a host such as a human being. The claim does not make it clear that the cell, even though it is a recombinant cell, is an isolated cell. Claims that read on a human being are considered non-statutory. Examiner

suggests amending the claim to recite "An isolated host cell transfected with..." to overcome the rejection.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> **The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.**

Claims 73 and 75 and claims 74 and 76, 80, 85 and 89 depending therefrom are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 73 and 75 recite the phrase "an amino acid sequence as depicted in SEQ ID NO:2" and "a nucleotide sequence as depicted in SEQ ID NO:1". The metes and bounds of these phrases in the context of the above claims are not clear to the Examiner. It is not clear whether the polypeptide comprises a fragment of SEQ ID NO:2 or the full length of the amino acid sequence of SEQ ID NO:2. Similarly, it is not clear whether the polynucleotide comprises a fragment of SEQ ID NO:1 or the full length of the nucleotide sequence of SEQ ID NO:1. A perusal of the specification did not provide the Examiner with a specific definition for the above phrases. As applicants have not provided a definition for the above phrase, Examiner has interpreted the claims broadly to mean that a polypeptide comprising "an amino acid depicted in SEQ ID NO:2" encompasses fragments of SEQ ID NO:2 and that a polynucleotide comprising "a nucleotide sequence depicted in SEQ ID NO:1" encompasses fragments of SEQ ID

NO:1. Examiner requests clarification of the above phrase and suggests amending the claim by replacing "an" with "the" in the above phrases.

Claims 70, 73, 75, 90 and 95 and claims 71, 76, 78, 80, 83, 85, 87, 89 and 91-94 depending therefrom are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 70, 73, 75, 90 and 95 recite the phrase "depicted in". The metes and bounds of the phrase in the context of the claims are not clear. It is not clear to the Examiner if the recited polypeptide has the amino acid sequence of SEQ ID NO:2 or is a representative member of a genus. Similarly, it is not clear to the Examiner if the recited polynucleotide has the nucleotide sequence of SEQ ID NO:1 or is a representative member of a genus. Examiner suggests amending the phrase as "the amino acid sequence of SEQ ID NO:2" or "the nucleotide sequence of SEQ ID NO:1" to clearly indicate that the polypeptide recited in the claims has the amino acid sequence of SEQ ID NO:2 and that the polynucleotide recited in the claims has the nucleotide sequence of SEQ ID NO:1.

Claims 90 and 95 and claims 91-94 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 90 and 95 recite the phrase "hybridizes ... under conditions that afford levels of hybridization equivalent to those observed under either of these two conditions". The metes and bounds of the phrase are not clear in the context of the claims. It is not clear to the Examiner as to what hybridization conditions are encompassed in the phrase because it is also not clear to the Examiner as to what "levels of hybridization" compared to hybridization under conditions of 0.2x SSC at 68C and 50% formamide, 4xSSC at 42C is considered as "equivalent". Examiner requests clarification of the above phrase.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 90-95 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 90-95 are drawn to oligonucleotide of no more than 100 nucleotides, wherein said oligonucleotides comprise or consists essentially of a sequence of at least 20 or consecutive nucleotides of SEQ ID NO:1. However, the oligonucleotides of claims 90-95 were not described in the application as originally filed nor in any of its parent applications. Therefore, claims 90-95 contain new matter.

Given this lack of description of the oligonucleotides in the claims, the specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that applicants were in possession of the inventions of claims 90-95 at the time of filing of the instant application.

Claims 90-95 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 90-95 are drawn to oligonucleotides comprising 20-100 nucleotides, wherein the oligonucleotides comprises of at least 20-30 consecutive nucleotides of SEQ ID NO:1 and hybridizes under the conditions recited in claim 90. Therefore, the claims are drawn to a genus of polypeptides having any function. There is no disclosure of any particular structure to function/activity relationship in the disclosed species.

The claims are drawn to many functionally unrelated oligonucleotides encompassed within the scope of these claims, including partial sequences. The genus of these oligonucleotides comprise a large variable genus with the potentiality of encoding many different polypeptides or having different types of activities by themselves or no activity. The specification, however, only provides the representative species of the oligonucleotides of SEQ ID NOs: 8-11. Therefore, there is no disclosure

of any particular structure to function/activity relationship in the disclosed species. The genus of oligonucleotides that are claimed is large variable genus with potentiality of comprising oligonucleotides having unknown function. The specification also fails to describe additional representative species of the oligonucleotides by any identifying characteristics or properties of the oligonucleotides other than the structural characteristics recited in the claims, for which no predictability of function is apparent. Given this lack of additional representative species as encompassed by the claims, applicants have failed to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize applicants were in possession of the claimed invention

Applicant is referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

In response to the previous Office Action, applicants have traversed the above rejection. Examiner notes that the rejection has been amended in response to the amendment of the claims.

Applicants argue that since the claims now recite that limitation of hybridizing to SEQ ID NO:1 under highly stringent conditions, the genus of oligonucleotides that fall within the scope of these claims is restricted to that subset of oligonucleotides that possess the claimed structure and function, that is, that comprising or consisting essentially of at least 20 consecutive nucleotides of SEQ ID NO:1 and that are capable of hybridizing under highly stringent conditions. Examiner respectfully disagrees. The

limitation of the oligonucleotides hybridizing under stringent conditions as recited in claim 90 do not provide any functional information on the claims oligonucleotides. Also, as discussed in the written description guidelines, the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. A representative number of species means that the species which are adequately described are representative of the entire genus. **Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus.** Satisfactory disclosure of a representative number depends on whether one of skill in the art would recognize that the applicant was in possession of the necessary common attributes or features of the elements possessed by the members of the genus in view of the species disclosed. For inventions in an unpredictable art, adequate written description of a genus which embraces widely variant species cannot be achieved by disclosing only one species within the genus. In the instant case the claimed genus includes species which are widely variant in function. The genus of claims 90-95 is functionally diverse as it encompasses oligonucleotides having no or unknown activity. As such, the disclosure

ofsolely structural features present in all members of the genus is insufficient to be representative of the attributes and features of the entire genus.

Applicants also argue that that since the specification describes hybridization of nucleic acids under highly stringent conditions requiring a substantial degree of sequence identity, nucleic acids that are structurally and, consequently, "functionally unrelated" are excluded. Examiner respectfully disagrees. The section of the specification applicants are referring to (page 19, lines 16-18) does not contain any such teaching, that nucleic acids that are "functionally unrelated" are precluded from the genus claimed. Even under highly stringent conditions, functionally unrelated oligonucleotides can bind to a given polynucleotide sequence. Applicants are asked to provide art teaching applicant's assertion that "functionally unrelated" sequences do not bind a given sequence.

Applicants also argue that according to both The Court of Appeals for the Federal Circuit and USPTO, nucleic acids based on their hybridization properties are adequately described if they hybridize under highly stringent conditions because such conditions dictate that all species within a genus will be structurally similar. Therefore, since the claimed oligonucleotides hybridize to SEQ ID NO:1 under highly stringent conditions as recited in claim 90, the claims are fully described. Examiner respectfully disagrees. The rejection is based on a genus comprising oligonucleotides having any function or no function, and not on a genus comprising oligonucleotides having any structure. Therefore, applicants' argument is immaterial.

Applicants argue that a oligonucleotide with 20-30 nucleotides of SEQ ID NO:1 and its inherent complement will hybridize to SEQ ID NO:1. It appears that applicants are arguing that the structure of the oligonucleotides are fully described, when the rejection is based on a genus comprising oligonucleotides having any function or no function.

Applicants also argue that since there is no basis in the statute or case law requiring some function or any function beyond that recited, speculation about the consequences of other functionality in the unrecited portion of the oligonucleotide has not place in a rejection for lack of written description and one must only describe what is claimed. Contrary to applicants' argument, no function for the oligonucleotides is recited in the claims. An oligonucleotide hybridizing to SEQ ID NO:1 does not describe a function for the oligonucleotide. If this were the case, then any string of nucleotides that happen to hybridize to a given polynucleotide sequence has function. Further, the rejection does not speculate about the consequences of other functionality, but addresses the lack of the description of the function of the claimed oligonucleotides.

Applicants also argue that since the PTO does not reject vectors or host cells for encompassing any function, the rejection is legally erroneous. Examiner respectfully disagrees. Vectors and host cells are indeed rejected for lacking written description if they comprise polynucleotides encoding polypeptides having no or unknown function. Further, if the function of the encoded polypeptides is recited in the claims, vectors and host cells are not rejected for encompassing any function or no function because the

recitation of its name "vector" and "host cell" inherently carry a function. The mere recitation of "oligonucleotide" does not impart any functionality to said oligonucleotide.

Hence the rejection is maintained.

Claims 70, 78, 83, 87 and 90-95 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a polynucleotide encoding the EER-7 of SEQ ID NO:2, vectors and host cells comprising said polynucleotide and a method of producing said EER-7 protein, does not reasonably provide enablement for (A) polynucleotides encoding EER-7 and further comprising four copies of a scavenger receptor cysteine rich domain (SRCR) having at least 80% sequence identity to any one of SEQ ID NOs: 3-6 or (B) oligonucleotides comprising 20--100 nucleotides, wherein the oligonucleotides comprises of at least 20-30 consecutive nucleotides of SEQ ID NO:1 and hybridizes under the conditions recited in claim 18 . The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required, are summarized in In re Wands (858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir. 1988)) as follows: (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in

the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claim(s).

Claims 70, 78, 83, 87 and 90-95 are drawn to polynucleotides encoding EER-7 and further comprising four copies of a scavenger receptor cysteine rich domain (SRCR) having at least 80% sequence identity to any one of SEQ ID NOs: 3-6 and oligonucleotides comprising 20-100 nucleotides, wherein the oligonucleotides comprises of at least 20-30 consecutive nucleotides of SEQ ID NO:1 and hybridizes under the conditions recited in claim 90. The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of polynucleotides encoding SEQ ID NO:2 further comprising any or all fragments, mutants and recombinants of SRCR and oligonucleotides comprising 20-30 consecutive nucleotides of SEQ ID NO:1 and any 20-80 nucleotides, wherein said oligonucleotides hybridize to SEQ ID NO:1 under conditions recited in claim 90, broadly encompassed by the claims.

Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function. However, in this case the disclosure is limited to the polynucleotide encoding the EER-7 protein of SEQ ID NO:2 having lysyl oxidase activity and the oligonucleotides consisting

of SEQ ID NOs: 8-10 or 11. It would require undue experimentation of the skilled artisan to make and use the claimed polynucleotides and oligonucleotides. In view of the great breadth of the claim, amount of experimentation required to make and used the claimed polynucleotides and oligonucleotides, the lack of guidance, working examples, and unpredictability of the art in predicting function from a polypeptide primary structure the claimed invention would require undue experimentation. As such, the specification fails to teach one of ordinary skill how to use the full scope of the polynucleotides encompassed by this claim.

Regarding the oligonucleotides, since the specific nucleotide sequence determines its structural and functional properties as primer/probe/antisense, predictability of which changes can be tolerated in the oligonucleotide sequence and obtain the desired activity requires a knowledge of and guidance with regard to which nucleotide in the sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the oligonucleotides' structure relates to its function. While DNA isolation techniques, recombinant and mutagenesis techniques are known, and it is routine in the art to screen for multiple substitutions or multiple modifications as encompassed by the instant claims, the specific nucleotide positions within oligonucleotides where modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited and the result of such modifications is unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given nucleotide sequence to diminish with each further

Since the scope of the claims require an undue experimentation to make and use the claimed polynucleotides, the claims are also not commensurate with the enablement provided by the disclosure with regard to inoperative embodiments encompassed by the claims, fragments, including mutants, variants and recombinants, of SEQ ID NO:1 having any structure with an unknown use. Although the presence of inoperative embodiments within the scope of the claims does not necessarily render a claim non-enabled, the standard is whether a skilled person could determine which embodiments that were conceived, but not yet made, would be inoperative or operative with expenditure of no more effort than is normally required in the art. *Atlas Powder Co. v. E.I. du Pont de Nemours & Co.*, 750 F.2d 1569, 1577, 224 USPQ 409, 414 (Fed. Cir. 1984). The scope of the claims are not enabled when undue experimentation is involved in determining those embodiments that are operable. In the instant case, the claims read on significant numbers of inoperative embodiments, rendering the claims non-enabled, since the specification does not clearly identify the operative embodiments and undue experimentation is involved in determining those that are operative. *Atlas Powder Co. v. E.I. duPont de Nemours & Co.*, 750 F.2d 1569, 1577, 224 USPQ 409, 414 (Fed. Cir. 1984); *In re Cook*, 439 F.2d 730, 735, 169 USPQ 298, 302 (CCPA 1971).

The specification does not support the broad scope of the claims which encompass polynucleotides encoding SEQ ID NO:2 further comprising any or all fragments, mutants and recombinants of SRCR having 80% identity to SEQ ID NOs: 3-6 and comprising of four SRCR domains having any one of SEQ ID NOs: 3-6 and oligonucleotides comprising of 1-100 nucleotides comprising of any 20-30 consecutive

nucleotides of SEQ ID NO:1 and hybridizing to SEQ ID NO:1 because the specification does not establish: (A) regions of the encoded EER-7 protein structure which may be modified without affecting lysyl activity; (B) the general tolerance of EER-7 proteins to modification and extent of such tolerance; (C) a rational and predictable scheme for adding variants, mutants and recombinants of SEQ ID NO:3-6 to either terminus of SEQ ID NO:2 with an expectation of obtaining the desired biological function, a EER-7 protein having lysyl activity; (D) rational and predictable scheme for modifying any amino acid residue with an expectation of obtaining the desired biological function; (E) regions of SEQ ID NO:1 which may by modified to use as primers or probes; (B) the general tolerance of such sequences to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any nucleotide in the sequence with an expectation of obtaining the desired biological function; and (F) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

The claims are drawn to oligonucleotides having unknown function. Therefore, the breadth of these claims is much larger than the scope enabled by the specification. The function of oligonucleotides cannot be predicted from its structure and the specification does not teach how to use oligonucleotides having any function or having no activity. The quantity of experimentation in this area is extremely large since there is significant variability in the activity of the oligonucleotide in the claims. It would require significant study to identify the actual function of the oligonucleotide and identifying a use for the oligonucleotide or their encoded polypeptides, if they exist, would be an

inventive, unpredictable and difficult undertaking. This would require years of inventive effort, with each of the many intervening steps, upon effective reduction to practice, not providing any guarantee of success in the succeeding steps.

The art is extremely unpredictable with regard to protein function in the absence of realizable information regarding its activity. Even very similar proteins may have every different functions. In the current case, where no specific information is known regarding the function, it is entirely unpredictable what function and activity will be found for the protein. The prior art does not resolve this ambiguity, since no prior art activity is identified for the encoded polypeptides.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including polynucleotides encoding EER-7 proteins further comprising SRCR having 80% sequence identity to SEQ ID NOs: 3-6, including any or all variants, recombinants and mutants thereof, and oligonucleotides comprising of 20-100 nucleotides comprising any 20-30 consecutive nucleotides of SEQ ID NO:1 and any 20-80 nucleotides, wherein the oligonucleotides have any function or unknown function. The scope of the claims must bear a reasonable correlation with the scope of enablement (*In re Fisher*, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of polynucleotides encoding EER-7 having the desired biological characteristics and determination of oligonucleotides comprising any 20-30 consecutive nucleotides of SEQ ID NO:1 are unpredictable and the experimentation left to those

skilled in the art is unnecessarily, and improperly, extensive and undue. See *In re Wands* 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

In response to the previous Office Action, applicants have traversed the above rejection. Examiner notes that the rejection has been amended in response to the amendment of the claims.

Applicants argue that the polynucleotides of claims 70, 78, 83 and 87 are fully enabled by the specification because the claims are now drawn to a polypeptide having at least 95% sequence similarity to SEQ ID NO:2. Examiner respectfully disagrees. Contrary to applicants' argument, the claims 70, 78, 83 and 87 are drawn to a polynucleotide having 95% sequence similarity to SEQ ID NO:2 and <u>further comprising</u> four SRCR domains having at least 80% sequence identity to SEQ ID NO:3-6 and SEQ ID NO:7. The claims encompass polynucleotides encoding SEQ ID NO:2 <u>further comprising any or all fragments, mutants and recombinants of SRCR</u> . As discussed above, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires a specific knowledge of and guidance with regard to which specific amino acids in the protein's sequence, can be modified such that the modified polypeptide continues to have said claimed activity. It is this specific guidance that applicants do not provide. Without specific guidance, those skilled in the art will be subjected to undue experimentation of making and testing each of the enormously large number of mutants that results from such experimentation. While the art may teach in general the structure of EER-7, conserved amino acid

sequences, and etc, such teachings will not reduce the burden of undue experimentation on those of ordinary skill in the art.

Applicants also argue that the oligonucleotides of claims 90-95 are fully enabled by the specification because the claims are now drawn to a oligonucleotides comprising at least 20-30 consecutive nucleotides of SEQ ID NO:1 that hybridizes under highly stringent conditions. Examiner respectfully disagrees. The claims are not drawn to primer or probes consisting of 20 or 30 consecutive nucleotides of SEQ ID NO:1 but oligonucleotides comprising 20 or 30 consecutive nucleotides of SEQ ID NO:1 and any 70-80 nucleotides, wherein said oligonucleotides have any or unknown function. The limitation of the oligonucleotides hybridizing under stringent conditions as recited in claim 90 do not provide any structural or functional information on the 70-80 nucleotides comprised in the oligonucleotide.

Applicants also argue that oligonucleotides that do not hybridize under the recited conditions are not within the scope of the claims and therefor enablement for such oligonucleotides is not at issue. However, since the claims are not drawn to primer or probes consisting of 20 or 30 consecutive nucleotides of SEQ ID NO:1 hybridizing to SEQ ID NO:1, but the claims are drawn to oligonucleotides comprising 20 or 30 consecutive nucleotides of SEQ ID NO:1, wherein the claimed oligonucleotides comprise any 70-80 nucleotides. The claims are not commensurate with the enablement provided by the disclosure with regard to inoperative embodiments encompassed by the claims, fragments, including mutants, variants and recombinants, of SEQ ID NO:1 having any structure with an unknown use. Although the presence of

inoperative embodiments within the scope of the claims does not necessarily render a claim non-enabled, the standard is whether a skilled person could determine which embodiments that were conceived, but not yet made, would be inoperative or operative with expenditure of no more effort than is normally required in the art. In the instant case, there is undue experimentation in determining those embodiments that are operable because the claims read on significant numbers of inoperative embodiments, rendering the claims non-enabled, since the specification does not clearly identify the operative embodiments, the 70-80 nucleotides comprised in the oligonucleotides, and undue experimentation is involved in determining those that are operative.

Applicants also argue that if the oligonucleotide is larger than 20 nucleotide, the additional sequence may be fully or partially complementary to SEQ ID NO:1, so as to contribute to hybridization, or it may provide some other functionality, such as a ribosome, therefore, the claims are enabled. Examiner respectfully disagrees. (It appears applicants meant to say "ribozymes" instead of "ribosomes".) Since the specific nucleotide sequence determines its structural and functional properties as primer/probe/antisense, predictability of which changes can be tolerated in the oligonucleotide sequence and obtain the desired activity requires a knowledge of and guidance with regard to which nucleotide in the sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the oligonucleotides' structure relates to its function. It is this specific guidance that applicants do not provide. Without specific guidance, those skilled in the art will be subjected to undue experimentation of making

and testing each of the enormously large number of mutants that results from such experimentation.

Applicants also argue that since the claims have been amended to recite that the oligonucleotides hybridize under highly stringent conditions to SEQ ID NO:1, the 20 nucleotides of said oligonucleotides will hybridize with a high degree of specificity and consequently, these claims do not contemplate such a wide range of polynucleotides. Examiner respectfully disagrees. The claims are drawn to oligonucleotides comprising 20 or 30 consecutive nucleotides of SEQ ID NO:1 and any 70-80 nucleotides, wherein said oligonucleotides have any or unknown function. The limitation of the oligonucleotides hybridizing under stringent conditions as recited in claim 90 do not provide any structural or functional information on the 70-80 nucleotides comprised in the oligonucleotide.

Applicants also argue that the claims are enabled because oligonucleotide hybridization is a well established phenomenon that is routinely used in the field of molecular biology and the amount of experimentation necessary to make and use the claimed oligonucleotide is routine, given the guidance in the specification and claims, the state of the art, and the high level of skill in the art. Examiner respectfully disagrees. While making oligonucleotides from a given polynucleotide may be routine in the art, the claims encompass an extremely large number of oligonucleotides. It would require undue experimentation of the skilled artisan to use oligonucleotides that consists of 20-100 nucleotides comprising any 70-80 nucleotides that also hybridizes to SEQ ID NO:1 under highly stringent conditions.

Hence the rejection is maintained.

Allowable Subject Matter

Claims 69, 72 and 77 are allowable.

Claims 86 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Yong Pak whose telephone number is 571-272-0935. The examiner can normally be reached 6:30 A.M. to 5:00 P.M. Monday through Thursday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy can be reached on 571-272-0928. The fax phone numbers for the organization where this application or proceeding is assigned are 571-273-8300 for regular communications and 703-872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 571-272-1600.

Yong D. Pak
Patent Examiner 1652

Manjunath Rao
Primary Examiner 1652